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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,394	05/16/2001	Naoto Miwa	SCH 1799	2377

23599 7590 08/25/2006

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EXAMINER	
CAPPS, KEVIN J	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 08/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/787,394	MIWA ET AL.	
	Examiner	Art Unit	
	Kevin J. Capps	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31,32,36-42 and 46-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31,32,36-42 and 46-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/23/05; 1/23/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on January 23, 2005, has been entered.

Status of the Claims

2. A Notice of Appeal was filed in the instant application on November 23, 2005, in response to the Advisory Action mailed on December 14, 2005. The amendments to the claims filed on November 23, 2005, have been entered. A Request for Continued Examination (RCE) was subsequently filed on January 23, 2006. Thus, as indicated above, the appeal has been withdrawn and prosecution in this application has been reopened. After the filing of the RCE, a Restriction Requirement was mailed on April 10, 2006. Applicant's agent, Casaba Henter, held a telephonic interview with the previous Examiner on May 25, 2006, discussing the Restriction Requirement and the Advisory Action mailed on December 14, 2005. According to the Interview Summary, the Examiner indicated the allowability of method claims "to the extent that they read on the

elected species". Applicant then submitted a Response to the Restriction Requirement and Amendments to the claims in order to "amend the claims to the allowable matter described in the interview summary." However, after reviewing the application file, the new Examiner feels that the claims are not in condition for allowance and the previous Examiner's indication of allowability is hereby withdrawn. Thus, the amended and new claims 31, 32, 36-42, and 46-53 filed in response to the Restriction Requirement mailed on April 10, 2006, are pending and examined on the merits herein.

Information Disclosure Statement

3. The information disclosure statements (IDSs) filed on November 23, 2005, and January 23, 2006, are in compliance with the provisions of 37 CFR 1.97. Accordingly, the IDSs are being considered by the Examiner.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 31, 32, 36-42, and 46-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Licha et al. (US 6,083,485 and/or US 6,258,340. Both documents contain the same disclosure. Citations refer to '485 unless specifically noted otherwise.)

7. Licha et al. teach a method of in vivo imaging comprising administering a genus of compounds that encompasses compounds of the instant formula III-1 (claim 1 of '340; col. 4, line 64-col. 6, line 14). Licha et al. teach that the compounds can have sulfonic acid groups (see, for example, col. 5, line 21). Licha et al. teach that the compounds can be administered in combination with a pharmaceutically acceptable carrier (col. 14, lines 41-52). Licha et al. teach that the in vivo imaging method is for angiography and tumor imaging (col. 1, line 66-col. 2, line 6; col. 9, lines 30-34; col. 13, lines 26-31).

8. Licha et al. do not exemplify compounds of the instant formula III-1 as preferred for use in the in vivo imaging method. Licha et al. do not teach that when a compound containing a sulfonic acid group is selected from within their genus of compounds for use in the in vivo imaging method, the sodium salt of the sulfonic acid substituent is preferred.

9. It would have been obvious to the person of ordinary skill in the art at the time of invention to administer the compounds of the instant formula III-1 in a method of in vivo imaging for angiography and/or tumor imaging. It would have further been obvious to administer the compounds of the instant formula III-1 as sodium salts.

10. The person of ordinary skill in the art would have been motivated to administer the compounds of the instant formula III-1 for in vivo imaging because Licha et al. teach a genus of compound encompassing the instant compounds that are effective for in vivo imaging of blood flow and tumors. Because Licha et al. teach that the entire genus of compounds is effective for in vivo imaging, the person of ordinary skill in the art would have expected that any of the compounds selected from within the genus disclosed by Licha et al., including the compounds of the instant formula III-1, would be effective for in vivo imaging. Further, it has been established that it is obvious to form a salt from a known acid. *In re Williams*, 89 USPQ 396 (CCPA 1951). Thus, it would have been obvious to the person of ordinary skill in the art to administer the sulfonic acid-containing compounds of Licha et al. as sodium salts in imaging methods.

11. Claims 31, 32, 36-42, and 46-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Licha et al. as applied to claims 31, 32, 36-42, and 46-53 above, and further in view of Ohno et al. (US 4,839,265).

12. As discussed above, Licha et al. teach in vivo imaging methods for angiography and tumor imaging comprising administering a genus of compounds encompassing compounds of the instant formula III-1.

13. Licha et al. do not exemplify compounds of the instant formula III-1 as preferred for use in the in vivo imaging method. Licha et al. do not teach that when a compound containing a sulfonic acid group is selected from within their genus of compounds for

use in the in vivo imaging method, the sodium salt of the sulfonic acid substituent is preferred.

14. Ohno et al. teach compounds within the scope of the compounds administered in the imaging method of Licha et al. that are also within the scope of the instant formula III-1. Notably, Ohno et al. exemplify sodium salts of these compounds (see: compounds (I-3), (I-5), (I-7), (I-11), and (I-12); col. 3, lines 19-25). Ohno et al. teach that the compounds are photosensitive and that they are dyes.

15. It would have been obvious to the person of ordinary skill in the art at the time of invention to administer the compounds exemplified by Ohno et al. as the sodium salts, which are within the genus of compounds taught by Licha et al., in a method of imaging for angiography and/or tumor imaging, to arrive at the instantly claimed method.

16. The person of ordinary skill in the art would have been motivated to administer the compounds of Ohno et al. for in vivo imaging because Ohno et al. exemplify compounds of the instant formula III-1 that are within the genus of compounds taught by Licha et al. that are effective for in vivo imaging of blood flow and tumors, and Ohno et al. also teach how to make the compounds, i.e., obtain the compounds. Further, the person of ordinary skill in the art would have been motivated to administer the compounds of Ohno et al. in the method of Licha et al. because Ohno et al. teach that the compounds are photosensitive and they are dyes. Therefore the person of ordinary skill in the art would have expected them to be effective in the method of imaging taught by Licha et al. Because Licha et al. teach that the entire genus of compounds encompassing the compounds of the instant formula III-1 is effective for in vivo imaging,

the person of ordinary skill in the art would have expected that any of the compounds selected from within the genus disclosed by Licha et al., including the compounds exemplified by Ohno et al., would be effective for in vivo imaging.

Response to Arguments

17. Applicant's arguments filed November 23, 2005, have been considered but they are not found persuasive. Applicant argues that "the one compound the examiner relies on from Ohno is a multipotassium salt. The claims of this application recite only sodium salts." (p. 7 of Remarks filed November 23, 2005). Applicant further argues that claims directed only to sodium salts are not obvious in view of the cited references because of the low toxicity of the sodium salts of compounds of formula III-1 compared to the corresponding potassium salts. Applicant cites the toxicity data for the compounds shown on p. 84 of the instant application, which was also resubmitted with the Remarks filed on April 12, 2004, as evidence of unexpected results associated with the sodium salts of the compounds. Applicant states, "Because the properties are clearly significant (toxicity being a main consideration for any compound to be administered to a live body), and unexpected, if there were a prima facie case of obviousness, the data of record would firmly rebut it." (p. 7 of Remarks filed November 23, 2005). Applicant also argues that a person of ordinary skill in the art would not have been motivated to select a compound from Ohno et al. because it is not analogous art.

18. Applicant's arguments are not found persuasive for the following reasons. First, as discussed above, Ohno et al. do in fact exemplify sodium salts of the genus of

compounds taught by Licha et al. Although Ohno et al. do not teach the compounds for use in in vivo imaging, they teach that the compounds are photosensitive and that they are dyes. Thus, as discussed above, because Licha et al. teach a genus of compounds that are useful for in vivo imaging, and Ohno et al. teach specific compounds within the genus disclosed by Licha et al. that are photosensitive, the person of ordinary would have been motivated with a reasonable expectation of success to use the compounds exemplified by Ohno et al., including the sodium salts, for in vivo imaging.

19. The toxicity data for the sodium salts of the compounds of formula III-1 has been considered, but the data is not considered to be significant to the instantly claimed method. It is noted that it is Applicant's burden to demonstrate unexpected results over the prior art. See MPEP § 716.02, particularly § 716.02 (a) - (g). The unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" (*In re Lohr*, 137 USPQ 548 (CCPA 1963)), and be of a scope reasonably commensurate with the scope of the subject matter claimed (*In re Linder*, 173 USPQ 356 (CCPA 1972)). The toxicity data supplied in the Remarks filed on April 12, 2004, for compounds (31), (43), and (45) is said to be >3550, 1630, and 1100-1220 mg/kg respectively for the sodium salts, and 350, 300-350, and 550 mg/kg respectively for the potassium salts. Although this data does indicate a lower toxicity for the sodium salts relative to the potassium salts, this result is not seen to be significant or practical in the context of the instantly claimed

method. By Applicant's own reasoning, the significance of the result is that the compounds are to be administered to a live body, and toxicity is a "main consideration for any compound to be administered to a live body". Thus, in order to be significant, the toxicity data should be relevant to the amount of the compounds to be administered in the method, i.e., the toxicity matters only if the compounds are to be administered in that dose range. In Example 4 on pp. 82-83 of the instant specification, Applicant demonstrates that the compounds are administered for in vivo imaging at a dose of 5.0 mg/kg, which is far below the toxicity levels of both the sodium and potassium salts. Thus the showing of the lower toxicity of the sodium salts of compound III-1 relative to the potassium salts is not of practical significance because the compounds are administered at levels far below the toxicity levels of both series of compounds for imaging purposes.

Double Patenting

20. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

21. Claims 31, 32, 36-42, and 46-53 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 35-44 of copending Application No. 10/324,010. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to methods of using the same compounds for in vivo imaging.

22. '010 teaches a method of imaging in a living body comprising administering compounds that overlap in scope with the compounds administered in the instantly claimed method.

23. '010 does not teach all of the herein-claimed preferred compounds.

24. It would have been obvious to the person of ordinary skill in the art to select the instant compounds of formula III-1 and to administer them in a method of imaging, particularly for angiography or tumor imaging.

25. The person of ordinary skill in the art would have been motivated to select the compounds of the instant formula III-1 and administer them for imaging because they are within the scope of the compounds taught in '010, and '010 teaches that all of the compounds are effective for imaging. Thus, the person of ordinary skill in the art would have expected success administering any of the compounds taught in '010 for imaging because they are taught to be equivalents for imaging purposes.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

26. Claims 31, 32, 36-42, and 46-53 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim16-22 and 24-26 of copending Application No. 10/419,917. Although the conflicting claims are not identical, they are not patentably distinct from each other because '917 anticipates the instantly claimed method.

27. '917 teaches a method of imaging for angiography and/or tumor imaging comprising administering a compound within the scope of the instantly claimed method (see the first compound of claim 1). Thus, '917 anticipates the instantly claimed method.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

28. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin J. Capps whose telephone number is (571) 272-8646. The examiner can normally be reached on Monday-Friday, 7:30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

KC

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER